the mutagenicity of the unfractionated sample. A reconstructed mixture was made by combining fractions in the proportions in which they were recovered. The mutagenic activity of the PDU-9 reconstruction was less than the unfractionated PDU-9 mutagenicity and was roughly equivalent to the sum of fraction mutagenicities. Assay of Lum. Prod. and Lum. Feed, however, suggest not only loss of activity as a result of fractionation, but also interactions among fraction components contributing to mutagenicity. PDU-9 hexane-extractable-materials were found to reduce the mutagenicity of benzo(a)pyrene and to enhance the mutagenicity of 2-aminoanthracene. Supported by Grant No. DE-AC22-83PC62999.

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THE MECHANISM OF POTENTIATION BY INHIBITORS OF POLY (ADP-RIBOSE) SYNTHESIS OF CARCINOGEN-INDUCED SISTER CHROMATID EXCHANGES. Jeffrey L. Schwartz, Department of Radiation Oncology, University of Chicago, Chicago, IL 60637.

3-Aminobenzamide (3AB), a potent inhibitor of poly (ADP-ribose) synthesis, will increase the baseline frequency of sister chromatid exchanges (SCEs) in exposed cells as well as potentiate the frequency of SCEs induced by certain monofunctional alkylating agents. Experiments were carried out in CHO cells to determine if 3AB interacts preferentially with alkylation-induced DNA strand breaks or some other alkylated DNA lesion in the induction of SCEs. The magnitude of the 3AB-mediated potentiation of SCE induction was not directly related to either the number of DNA strand breaks produced by the alkylating agent or the alkylation-induced SCE frequency. Instead, the potentiation of SCE frequency was related to the degree of membrane damage produced. Furthermore, the potentiation of SCE frequency was reversed by the addition of NAD^+ to the medium. NAD^+ is the substrate for ADP-ribosylation. These results suggest that the interaction between 3AB and certain alkylating agents in SCE formation is due to cell membrane permeabilization and the loss of intracellular NAD^+. Thus the interaction between 3AB and certain carcinogenic agents in SCE formation is a much different process than that which results in increased cytotoxicity, mutagenicity and carcinogenicity.

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CONCLUSIVE DETERMINATION OF THE MUTAGENICITY OF SINGLET OXYGEN. John Seed, Kathy Specht* and W. Robert Midden, Departments of Immunology and Infectious Diseases (JS) & Environmental Health Sciences (KS & WRM), The Johns Hopkins University, Baltimore, MD

Singlet oxygen ($^1\Delta_g$ O_2) is the lowest energy electronically excited state of molecular oxygen and represents a reactive form of molecular oxygen. $^1\Delta_g$ O_2 is generated by sunlight illumination of endogenous photosensitizers in the atmosphere, surface waters and soil. It can also be generated in human tissue by a number of photosensitizers including coal tar derivatives, rose bengal, methylene blue, acridines, hematoporphyrins and many other dyes and pigments and may be formed either directly or indirectly in lipid peroxidation induced by superoxide, hydrogen peroxide, hydroxyl radical and other redox active agents, as well as in the oxidative burst of polymorphonuclear leukocytes. Therefore $^1\Delta_g$ O_2 may be an important intermediate in the carcinogenesis and mutagenesis associated with frustrated phagocytosis and chronic inflammation. Because of its short lifetime ($\approx$ 3 µsec in H_2O) and the generation of other reactive intermediates by most methods used to produce $^1\Delta_g$ O_2, the determination of the role of $^1\Delta_g$ O_2 in mutagenesis is difficult and the results are often ambiguous. We will describe a new method that can be used to conclusively test the mutagenicity of $^1\Delta_g$ O_2. A separated-surface-sensitizer is used to generate $^1\Delta_g$ O_2 in these experiments and the role of $^1\Delta_g$ O_2 is demonstrated by determining the decrease in mutation frequency with increasing distance of separation of the sensitizer and the bacterial solution. We have used this method with an azaguanine resistance assay to test the ability of $^1\Delta_g$ O_2 to activate the mutagenicity of benzo[a]pyrenes in *Salmonella typhimurium*. Low doses of $^1\Delta_g$ O_2 increase the mutagenicity of 7,8-saturated benzo[a]pyrenes at least four fold over samples treated with light without sensitizer (no $^1\Delta_g$ O_2). Mutagenesis was not observed with benzo[a]pyrenes that are unsaturated at the 7,8-position. The $^1\Delta_g$ O_2 activation of the mutagenicity of 7,8-saturated benzo[a]pyrenes by $^1\Delta_g$ O_2 may represent a new biochemical pathway to benzo[a]pyrene mutagenesis and carcinogenesis. (Supported by NIEHS grant no. ES02300.)

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ETHYLENE OXIDE-INDUCED DNA BREAKAGE IN MOUSE GERM CELLS MEASURED BY ALKALINE ELUTION. G. A. Sega, and E. E. Generoso*, Biology Division, ORNL, Oak Ridge, TN 37831

Alkaline elution was used to assess the DNA breakage induced by ethylene oxide (EtO) in meiotic and postmeiotic germ-cell stages of male mice. Germ cells were labeled with [^{3}H]dThd and the mice were subsequently given a single i.p. injection of 100 mg EtO/kg. Germ cells of control animals were labeled with [^{14}C]dThd. At various times from 4h to 22d after EtO exposure, sperm were recovered from the vasa of treated and control animals,

Source: https://www.industrydocuments.ucsf.edu/docs/qflb0000